**DIVISION OF ANTIVIRAL PRODUCTS (HFD-530)**

**VIROLOGY REVIEW**

NDA: 208215  SDN: 001  DATE REVIEWED: 10/29/2015

Clinical Virology Reviewer: Lisa K. Naeger, Ph.D.

**NDA#: 208,215**  **Supporting Document #: 001**

Reviewer's Name(s): Lisa K. Naeger, Ph.D.

Applicant Name and Address:
Gilead Sciences, Inc.
333 Lakeside Drive
Foster City, CA 94404

Initial Submission Dates:
- Correspondence Date: 04/07/2015
- CDER Receipt Date: 04/07/2015
- Assigned Date: 04/07/2015
- Review Complete Date: 12/01/2015
- PDUFA Date: 04/07/2016

Amendments:

<table>
<thead>
<tr>
<th>SDN</th>
<th>CDER Stamp Date</th>
<th>Assigned Date</th>
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<td>006</td>
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<td>07/15/2015</td>
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<td>011</td>
<td>10/13/2015</td>
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<td>012</td>
<td>11/6/2015</td>
<td>11/9/2015</td>
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Related/Supporting Documents: NDA-207561 and NDA-21500

Product Name(s): emtricitabine and tenofovir alafenamide fumarate

Proprietary: DESCOVY

Non-Proprietary/USAN: FTC/TAF

<table>
<thead>
<tr>
<th>Individual Component</th>
<th>FTC</th>
<th>TAF</th>
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<tbody>
<tr>
<td>Structure</td>
<td><img src="image" alt="FTC Structure" /></td>
<td><img src="image" alt="TAF Structure" /></td>
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<tr>
<td>Chemical Names</td>
<td>L-Alanine,N-[(S)-[(1R)-2-(6-amino-9H-purin-9-yl)-1-methylethoxy]methyl][phenoxyphosphinyl]-,1-methylethyl ester,(2E)-2-butenedioate (1:1)</td>
<td></td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>C$<em>8$H$</em>{10}$FN$_3$O$_3$S</td>
<td>C$<em>{25}$H$</em>{33}$O$_9$N$_6$P</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>247.24</td>
<td></td>
</tr>
<tr>
<td>Drug Class</td>
<td>NRTI</td>
<td>NRTI</td>
</tr>
<tr>
<td>Supporting Document</td>
<td>IND 53971; NDA 21500;</td>
<td>IND 63737; IND 111007</td>
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</tbody>
</table>
Indication(s): Treatment of HIV-1
Dosage Form(s): Tablet (FTC 200 mg/ TAF 25 mg)
Route(s) of Administration: Oral
Recommended Dosage: One tablet taken once daily with food
Dispensed: Rx _X_ OTC ___ (Discipline relevant)

Abbreviations: AIDS, acquired immunodeficiency syndrome; ARV, antiretroviral; CC\textsubscript{50}, 50\% cytotoxic concentration; COBI, cobicistat; EC\textsubscript{50}, effective concentration inhibiting viral replication by 50\%; EVG, elvitegravir; FTC, emtricitabine; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; NDA, new drug application; NNRTI, HIV-1 non-nucleoside reverse transcriptase inhibitor; NRTI, HIV-1 nucleoside/nucleotide reverse transcriptase inhibitor; PBMC, peripheral blood mononuclear cell; PCR, polymerase chain reaction; PR, HIV-1 protease; QD, once daily; RT, HIV-1 reverse transcriptase; TAF, tenofovir alafenamide fumarate; TDF, tenofovir disoproxil fumarate; TFV, tenofovir (active moiety of the diester prodrugs TAF and TDF)

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EXECUTIVE SUMMARY

This NDA for a fixed dose combination of emtricitabine and tenofovir alafenamide fumarate is approvable as a part of a regimen for treatment of HIV-1 infection in adults and pediatric patients 12 years and older from a virology perspective. FTC/TAF is being approved based on bioavailability studies and links the efficacy of FTC/TAF to the efficacy studies of GENVOYA™ (EVG/COBI/FTC/TAF) in NDA207561 approved on November 5, 2015. Labeling negotiations were ongoing at the time of finalization of this review, so labeling is not included in this review and will be included in the CDTL review.

Please refer to NDA207561 for complete virology review of tenofovir alafenamide.

1. RECOMMENDATIONS
   1.1 RECOMMENDATION AND CONCLUSION ON APPROVABILITY:

   This NDA for a fixed dose combination of emtricitabine and tenofovir alafenamide fumarate is approvable from a virology perspective as a part of a regimen for treatment of HIV-1 infection.

   1.2. RECOMMENDATION ON PHASE 4 (POST-MARKETING) COMMITMENTS, AGREEMENTS, AND/OR RISK MANAGEMENT STEPS, IF APPROVABLE:

   There are no phase 4 recommendations for this application.

2. ADMINISTRATIVE
   2.1. Reviewer’s Signature(s)

   Lisa K. Naeger
   [Lisa K. Naeger, Ph.D.]
   Sr. Virologist, HFD-530

   2.2. Concurrence

   HFD-530/Micro TL Jules O’Rear Date 12/1/2015
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LISA K NAEGER
12/02/2015

JULIAN J O REAR
12/02/2015
# MICROBIOLOGY FILING CHECKLIST FOR NDA-208215

**NDA Number:** 208215  
**Applicant:** Gilead Sciences  
**Stamp Date:** April 7, 2015

**Drug Name:** FTC/TAF  
**NDA Type:** Original NDA

On **initial** overview of the NDA application for filing:

<table>
<thead>
<tr>
<th>Content Parameter</th>
<th>Yes</th>
<th>No</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the virology information (nonclinical and clinical) provided and described in different sections of the NDA organized in a manner to allow substantive review to begin?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Is the virology information (nonclinical and clinical) indexed, paginated and/or linked in a manner to allow substantive review to begin?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Is the virology information (nonclinical and clinical) legible so that substantive review can begin?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>On its face, has the applicant submitted cell culture data in necessary quantity, using necessary clinical and nonclinical strains/isolates, and using necessary numbers of approved current divisional standard of approvability of the submitted draft labeling?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Has the applicant submitted any required animal model studies necessary for approvability of the product based on the submitted draft labeling?</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Has the applicant submitted all special/critical studies/data requested by the Division during pre-submission discussions?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Has the applicant submitted the clinical virology datasets in the appropriate format as described in the relevant guidance documents and are the datasets complete?</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Has the applicant used standardized or nonstandardized methods for virologic outcome measures? If nonstandardized methods were used, has the applicant included complete details of the method, the name of the laboratory where actual testing was done and performance characteristics of the assay in the laboratory where the actual testing was done?</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Has the applicant submitted draft labeling consistent with current regulation, divisional and Center policy, and the design of the development package?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Has the applicant submitted annotated microbiology draft labeling consistent with current divisional policy, and the design of the development package?</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Have all the study reports, published articles, and other references been included and cross-referenced in the</td>
<td>X</td>
<td></td>
</tr>
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</table>

File name: 5_Microbiology Filing Checklist for a NDA 208215

Reference ID: 3760542
## MICROBIOLOGY FILING CHECKLIST FOR NDA-208215

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<th>Content Parameter</th>
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<th>Comments</th>
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<tr>
<td>annotated draft labeling or summary section of the submission?</td>
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<tr>
<td>12 Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?</td>
<td>X</td>
<td></td>
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</tr>
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</table>

### IS THE MICROBIOLOGY SECTION OF THE APPLICATION FILEABLE?

**Yes**

If the NDA is not fileable from the microbiology perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

---

Lisa K. Naeger 05/18/15  
Reviewing Microbiologist  

Jules O’Rear 05/19/15  
Microbiology Team Leader  

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File name: 5_Microbiology Filing Checklist for a NDA 208215
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LISA K NAEGER
05/20/2015

JULIAN J O REAR
05/20/2015